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(71) Applicant (*for all designated States except US*): FUJISAWA PHARMACEUTICAL CO., LTD. [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541 (JP).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): ISHIE, Masayuki [JP/JP]; 5-19-4, Shinkofudai, Toyono-cho, Toyono-gun, Osaka 563-01 (JP).

(74) Agent: SEKI, Hideo; Fujisawa Pharmaceutical Co., Ltd., Osaka Factory, 1-6, Kashima 2-chome, Yodogawa-ku, Osaka-shi, Osaka 532 (JP).

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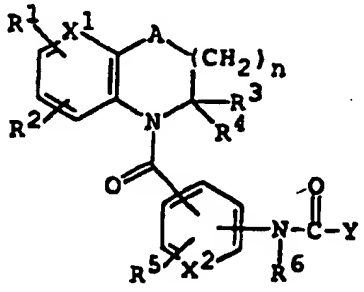
(54) Title: USE OF BENZAMIDE DERIVATIVES FOR TREATING AND/OR PREVENTING MENIERE'S SYNDROME AND MOTION SICKNESS

(57) Abstract

This invention relates to use of a compound of formula (I) wherein each symbol is as defined in the description, or its pharmaceutically acceptable salt, for treating and/or preventing Meniere's syndrome or motion sickness.



(I)

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USE OF BENZAMIDE DERIVATIVES FOR TREATING AND/OR PREVENTING MENIERE'S SYNDROME AND MOTION SICKNESS

TECHNICAL FIELD

This invention relates to a new use of benzamide derivatives which possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity or oxytocin antagonistic activity, for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness.

BACKGROUND ART

The benzamide derivatives used in this invention are known as described in European Patent Application Publication No. 0 620 216 that said benzamide derivatives possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity or oxytocin antagonistic activity and are useful in the treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, oxytocin relating diseases [e.g. premature delivery, dysmenorrhea, endometritis, etc.] and the like in human beings and animals.

DISCLOSURE OF INVENTION

This invention relates to a new use of benzamide derivatives, which possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells,

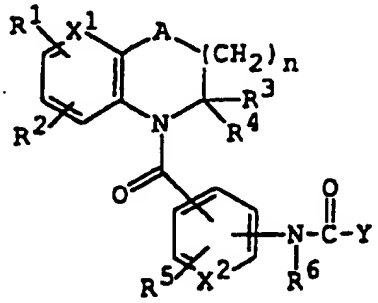
water diuretic activity, platelet agglutination inhibitory activity or oxytocin antagonistic activity, for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness.

Accordingly, this invention provides a new use of benzamide derivatives for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness.

Further, this invention provides an agent and a pharmaceutical composition for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness, which comprises said benzamide derivatives.

Still further, this invention provides a method for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness, which comprises administering said benzamide derivatives to mammals.

The benzamide derivatives used in this invention can be represented by the following general formula (I).



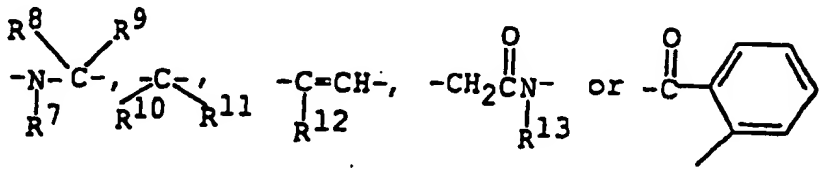
(I)

wherein R^1 is hydrogen or lower alkyl,
R^2 is hydrogen, lower alkyl, halo(lower)alkyl, halogen or lower alkoxy,
R^3 and R^4 are each hydrogen, lower alkyl or taken together to form oxo,
R^5 is hydrogen, halogen, nitro, hydroxy, protected hydroxy, lower alkyl or lower alkoxy optionally

substituted with lower alkylamino,

R^6 is hydrogen, lowing alkyl or acyl,

A is



in which

R^7 is hydrogen; lower alkyl optionally substituted with halogen, amino, lower alkylamino, protected amino, acyl, a heterocyclic group, hydroxy or protected hydroxy; or acyl; and

R^8 and R^9 are each hydrogen, or taken together to form oxo or thioxo; or

R^7 and R^8 are taken together to form a bond; and

R^9 is lower alkylamino, N-lower alkylpiperazinyl or lower alkylthio optionally substituted with lower alkylamino;

R^{10} is hydrogen;

R^{11} is hydrogen, hydroxy, lower alkylamino or lower alkyl optionally substituted with acyl; or

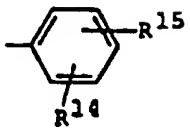
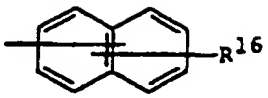
R^{10} and R^{11} are taken together to form oxo or lower alkoxyimino optionally substituted with acyl;

R^{12} is lower alkyl optionally substituted with acyl; and

R^{13} is lower alkyl;

X^1 is CH or N,

X^2 is CH or N,

Y is  or 

in which

R^{14} is hydrogen, halogen, hydroxy or lower alkoxy,

R^{15} is aryloxy, naphthyl, phenyl substituted with substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, halogen, halo(lower)alkyl, hydroxy, amino(lower)alkyl, azido(lower)alkyl, lower alkylamino(lower)alkyl, acylamino(lower)alkyl, hydroxy(lower)alkyl, cyano and acyl, or a heterocyclic group, and

R^{16} is aryl,

and

n is 0, 1, 2 or 3,

and pharmaceutically acceptable salts thereof.

Said compound (I) and pharmaceutically acceptable salts thereof are useful in the treatment and/or prevention of Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness in mammals.

Particulars of the various definitions mentioned in this specification and preferred examples thereof are explained in the following.

The term "lower" is intended to mean a group having 1 to 6 carbon atom(s), preferably one having 1 to 4 carbon atom(s), unless otherwise provided.

Suitable "lower alkyl" and lower alkyl moiety in the

terms "halo(lower)alkyl", "amino(lower)alkyl", "N-lower alkylpiperazinyl", "lower alkylthio", "N-lower alkyl-piperazinylcarbonyl", "lower alkylsulfonyl", "azido(lower)alkyl", "lower alkylamino(lower)alkyl", "acylamino(lower)alkyl", "hydroxy(lower)alkyl", "lower alkylcarbamoyl", "acyl(lower)alkyl" and "lower alkylamino" may be straight or branched one such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl or the like, in which preferable one is C_1-C_4 alkyl such as methyl, ethyl, propyl, isobutyl or tert-butyl.

Suitable "aryl" and aryl moiety in the terms "aryloxy" and "arylsulfonyl" may be phenyl, naphthyl, phenyl substituted with lower alkyl [e.g. tolyl, xylyl, mesityl, cumenyl, di(tert-butyl)pentyl, etc.] and the like, in which preferable one is phenyl or tolyl.

Suitable "halogen" may be fluorine, chlorine, bromine and iodine, in which preferable one is fluorine or chlorine.

Suitable "lower alkoxy" and lower alkoxy moiety in the term "lower alkoxyimino" may be methoxy, ethoxy, propoxy, isopropoxy, butoxy and the like, in which preferable one is methoxy or propoxy.

Suitable "lower alkylamino" may be mono or di(lower alkyl)amino such as methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, isobutylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, diisopropylamino, dipentylamino, dihexylamino, N-methylethylamino or the like, in which preferable one is dimethylamino.

Suitable "lower alkylamino(lower)alkyl" may be mono or di(lower alkyl)amino substituted lower alkyl such as methylaminomethyl, methylaminoethyl, methylaminopropyl, methylaminobutyl, methylaminohexyl, ethylaminomethyl, ethylaminoethyl, ethylaminopropyl, ethylaminobutyl, ethylaminohexyl, dimethylaminomethyl, dimethylaminoethyl, dimethylaminopropyl, dimethylaminobutyl, dimethylaminohexyl,

diethylaminomethyl, diethylaminoethyl, diethylaminopropyl, diethylaminobutyl, diethylaminohexyl or the like, in which preferable one is dimethylaminoethyl, dimethylaminopropyl or dimethylaminobutyl.

Suitable "halo(lower)alkyl" may be chloromethyl, fluoromethyl, bromomethyl, difluoromethyl, dichloromethyl, trifluoromethyl, trichloromethyl, 2-fluoroethyl and the like, in which preferable one is trifluoromethyl.

Suitable "heterocyclic group" and a heterocyclic moiety in the terms "a heterocyclic(lower)alkyl" and "a heterocycliccarbonyl" may be one containing at least one hetero atom selected from nitrogen, sulfur and oxygen atom, and may include saturated or unsaturated, monocyclic or polycyclic heterocyclic group, and preferable heterocyclic group may be N-containing heterocyclic group such as

unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl [e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.], tetrazolyl [e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.], etc.;

saturated 3 to 7-membered heteromonocyclic group containing 1 to 4 nitrogen atoms [e.g. pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, homopiperazinyl, etc.];

saturated heteropolycyclic group containing 1 to 4 nitrogen atoms, for example, quinuclidinyl, etc.;

unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g. tetrazolo[1,5-b]pyridazinyl, etc.], etc.;

unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, for example, pyranyl, furyl, etc.;

unsaturated, 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms, for example, thienyl, etc.;

unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl [e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.], etc.;
saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl, etc.];
unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzofurazanyl, benzoxazolyl, benzoxadiazolyl, etc.];
unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.], etc.;
saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl, etc.];
unsaturated condensed heterocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl, etc.];
unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms [e.g. benzofuranyl, benzodioxolyl, etc.] and the like.

Said "heterocyclic group" may be substituted with lower alkyl optionally substituted with hydroxy, acyloxy, amino, protected amino, acyl, aryl or methylenedioxyphenyl; acyl or a heterocyclic group, in which preferable one is piperazinyl, N-methylpiperazinyl, N,N-dimethylpiperazinyl, N-methylhomopiperazinyl, N-(2-hydroxyethyl)piperazinyl, N-(2-acetoxyethyl)piperazinyl, N-(3-phthalimidopropyl)-piperazinyl, N-(3-aminopropyl)piperazinyl, N-(pyrrolidinylcarbonylmethyl)piperazinyl, N-(methylenedioxyphenylmethyl)piperazinyl, N-ethoxycarbonylpiperazinyl, N-carboxypiperazinyl, N-tert-butoxycarbonylpiperazinyl, N-pyridylpiperazinyl,

dimethylaminopiperidyl, pyrrolyl, pyridyl, piperidyl, morpholinyl or quinuclidinyl.

Suitable "acyl" and acyl moiety in the terms "acylamino(lower)alkyl" and "acyl(lower)alkyl" may be carboxy, esterified carboxy, carbamoyl, lower alkylcarbamoyl, lower alkanoyl, aroyl, a heterocycliccarbonyl, lower alkylsulfonyl, arylsulfonyl and the like.

The esterified carboxy may be substituted or unsubstituted lower alkoxycarbonyl [e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, tert-butoxycarbonyl, hexyloxycarbonyl, 2-(dimethylamino)ethoxycarbonyl, 2-iodoethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, etc.], substituted or unsubstituted aryloxycarbonyl [e.g. phenoxycarbonyl, 4-nitrophenoxycarbonyl, 2-naphthyloxycarbonyl, etc.], substituted or unsubstituted ar(lower)alkoxycarbonyl [e.g. benzyloxycarbonyl, phenethyloxycarbonyl, benzhydryloxycarbonyl, 4-nitrobenzyloxycarbonyl, etc.] and the like, in which preferable one is lower alkoxycarbonyl or 2-(dimethylamino)ethoxycarbonyl.

The lower alkylcarbamoyl may be mono or di(lower)alkylcarbamoyl such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, dimethylcarbamoyl, diethylcarbamoyl, N-methyl-N-ethylcarbamoyl or the like.

The lower alkanoyl may be substituted or unsubstituted one such as formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl, hexanoyl, trifluoroacetyl or the like, in which preferable one is formyl or acetyl.

The aroyl may be substituted or unsubstituted one such as benzoyl, naphthoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl and the like.

The lower alkylsulfonyl may be methylsulfonyl, ethylsulfonyl, propylsulfonyl, butylsulfonyl and the like.

The arylsulfonyl may be substituted or unsubstituted one

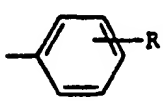
such as phenylsulfonyl, tolylsulfonyl, dimethoxyphenylsulfonyl or the like, in which preferable one is dimethoxyphenylsulfonyl.

"N-Protective group" in "protected amino" may be common N-protective group such as substituted or unsubstituted lower alkanoyl [e.g. formyl, acetyl, propionyl, trifluoroacetyl, etc.], phthaloyl, lower alkoxycarbonyl [e.g. tert-butoxycarbonyl, tert-amyloxycarbonyl, etc.], substituted or unsubstituted aralkoxycarbonyl [e.g. benzyloxycarbonyl, p-nitrobenzyloxycarbonyl, etc.], substituted or unsubstituted arenesulfonyl [e.g. benzenesulfonyl, tosyl, etc.], nitrophenylsulfenyl, aralkyl [e.g. trityl, benzyl, etc.] or the like, in which preferable one is phthaloyl or tert-butoxycarbonyl.

"Protected hydroxy" may be commonly protected hydroxy such as substituted lower alkoxy such as lower alkoxy(lower)alkoxy [e.g. methoxymethoxy, etc.], lower alkoxy(lower)alkoxy(lower)alkoxy [e.g. methoxyethoxymethoxy, etc.], substituted or unsubstituted ar(lower)alkoxy [e.g. benzyloxy, nitrobenzyloxy, etc.], etc., acyloxy such as lower alkanoyloxy [e.g. acetoxy, propionyloxy, pivaloyloxy, etc.], aroyloxy [e.g. benzoyloxy, fluorenecarbonyloxy, etc.], lower alkoxycarbonyloxy [e.g. methoxycarbonyloxy, ethoxycarbonyloxy, propoxycarbonyloxy, isopropoxycarbonyloxy, butoxycarbonyloxy, isobutoxycarbonyloxy, tert-butoxycarbonyloxy, pentyloxycarbonyloxy, hexyloxycarbonyloxy, etc.], substituted or unsubstituted ar(lower)alkoxycarbonyloxy [e.g. benzyloxycarbonyloxy, bromobenzyloxycarbonyloxy, etc.] etc., tri(lower)alkylsilyloxy [e.g. trimethylsilyloxy, etc.] and the like.

The phenyl group for R^{15} may be substituted with 1 to 5 substituent(s) as mentioned above, wherein the preferable number of the substituent(s) is 1 to 2.

Preferable compound (I) is one which has hydrogen for R^1, hydrogen, lower alkyl or halogen for R^2, hydrogen for R^3, hydrogen for R^4, hydrogen or lower alkoxy for R^5, hydrogen for R^6, $-N(R^7)-C(=O)-$ (wherein R^7 is lower alkyl optionally substituted with amino, lower alkylamino, protected amino, acyl or piperidino) or $-CH(R^{11})-$ (wherein R^{11} is hydrogen, lower alkylamino or acyl(lower)alkyl) for A, CH for X^1, CH for X^2,  (wherein R^{15} is phenyl substituted with substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, halogen, halo(lower)alkyl, hydroxy, amino(lower)alkyl, azido(lower)alkyl, lower alkylamino(lower)alkyl, acylamino(lower)alkyl, hydroxy(lower)alkyl, cyano and acyl) for Y, and 0, 1 or 2 for n.

More preferable compound (I) is one which has hydrogen for R^1, hydrogen, lower alkyl or halogen for R^2, hydrogen for R^3, hydrogen for R^4, hydrogen or lower alkoxy for R^5, hydrogen for R^6, $-N(R^7)-C(=O)-$ (wherein R^7 is lower alkyl substituted with N-lower alkylpiperazinylcarbonyl or lower alkyl substituted with di(lower)alkylamino) or $-CH(R^{11})-$ (wherein R^{11} is lower alkyl substituted with N-lower alkylpiperazinylcarbonyl) for A, CH for X^1, CH for X^2,  (wherein R^{15} is phenyl substituted with lower

alkyl or di(lower alkyl)) for Y, and 0, 1 or 2 for n.

Most preferable compound (I) is 5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one.

Suitable pharmaceutically acceptable salts of the compound (I) are conventional non-toxic salts and include an acid addition salt such as an inorganic acid addition salt [e.g. hydrochloride, hydrobromide, sulfate, phosphate, etc.], an organic acid addition salt [e.g. formate, acetate, trifluoroacetate, maleate, tartrate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.], a metal salt such as an alkali metal salt [e.g. sodium salt, potassium salt, etc.] and an alkaline earth metal salt [e.g. calcium salt, magnesium salt, etc.] and the like.

It is to be noted that the compound (I) may include one or more stereoisomer(s) such as optical isomer(s) and geometrical isomer(s) due to asymmetric carbon atoms and double bond(s), and all of such isomers and mixture thereof are included within the scope of this invention.

Now in order to show the utility of the compound (I) and pharmaceutically acceptable salts thereof in this invention, the test data of the representative compound of this invention is shown in the following.

Effect on Endocochlear Potential

1. Test Method:

Guinea-pigs were anesthetized with sodium pentobarbital (30mg/kg, i.p.). After tracheotomy, animals were maintained under artificial respiration. The cochlea was exposed using a ventrolateral approach. Endocochlear potential (EP) was recorded by means of a glass microelectrode inserted into the scala media. The Ag/AgCl reference electrode was placed on the exposed neck muscle.

Arginine vasopressin (AVP) and the test compound were

dissolved in saline. AVP (10^{-5}M), the test compound (0.1mg/ml), or both of them were administered through the vertebral artery. 2 ml of each drug solution was injected over a period of 2 minutes.

2. Test Compound:
5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-one (hereinafter referred to as Compound A)

3. Test Result:

Data was expressed as Change in EP (ΔEP, mV). AVP produced a large negative deflection of EP from +80 to +35mV, whereas simultaneous administration of AVP and FR161282 made no change in EP.

10^{-5}MAVP (ΔEP, mV)	0.1mg/ml Compound A (ΔEP, mV)	10^{-5}MAVP +0.1mg/ml Compound A (ΔEP, mV)
45	0	0

The result show that the compound (I) of this invention has an inhibitory activity against a negative deflection of endocochlear potential induced by arginine vasopressin and is useful for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness.

For therapeutic purpose, the compounds (I) and pharmaceutically acceptable salts thereof of the present invention can be used in a form of pharmaceutical preparation containing one of said compounds, as an active ingredient, in admixture with a pharmaceutically acceptable carrier such as an organic or inorganic solid or liquid excipient suitable for oral, parenteral or external (topical) administration.

The pharmaceutical preparations may be capsules, tablets, dragees, granules, solution, suspension, emulsion, ointment, or the like. If desired, there may be included in these preparations, auxiliary substances, stabilizing agents, wetting or emulsifying agents, buffers and other commonly used additives.

While the dosage of the compounds (I) will vary depending upon the age and condition of the pati80 to ent, an average single dose of about 0.1 mg, 1 mg, 10 mg, 50 mg, 100 mg, 250 mg, 500 mg and 1000 mg of the compound (I) may be effective for treating and/or preventing Meniere's syndrome (e.g. Meniere's disease, etc.) or motion sickness. In general, amounts between 0.1 mg/body and about 1,000 mg/body may be administered per day.

The following example is given for the purpose of illustrating the present invention.

Example 1

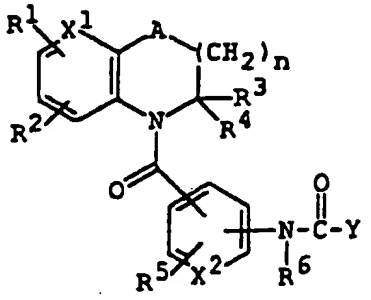
(Capsule)

5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-one	5 mg
Lactose	80 mg

The above-mentioned ingredients, were mixed and the mixture was encapsulated to provide the capsule.

CLAIMS

1. Use of a compound of the formula :



(I)

wherein R^1 is hydrogen or lower alkyl,

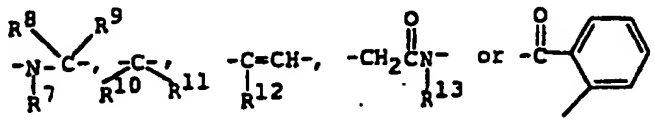
R^2 is hydrogen, lower alkyl, halo(lower)alkyl, halogen or lower alkoxy,

R^3 and R^4 are each hydrogen, lower alkyl or taken together to form oxo,

R^5 is hydrogen, halogen, nitro, hydroxy, protected hydroxy, lower alkyl or lower alkoxy optionally substituted with lower alkylamino,

R^6 is hydrogen, lower alkyl or acyl,

A is



in which

R^7 is hydrogen; lower alkyl optionally substituted with halogen, amino, lower alkylamino, protected amino,

acyl, a heterocyclic group, hydroxy or protected hydroxy; or acyl; and

R^8 and R^9 are each hydrogen, or taken together to form oxo or thioxo; or

R^7 and R^8 are taken together to form a bond; and

R^9 is lower alkylamino, N-lower alkylpiperazinyl or lower alkylthio optionally substituted with lower alkylamino;

R^{10} is hydrogen;

R^{11} is hydrogen, hydroxy, lower alkylamino or lower alkyl optionally substituted with acyl; or

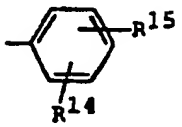
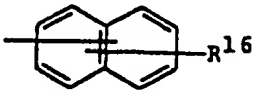
R^{10} and R^{11} are taken together to form oxo or lower alkoxyimino optionally substituted with acyl;

R^{12} is lower alkyl optionally substituted with acyl; and

R^{13} is lower alkyl;

X^1 is CH or N,

X^2 is CH or N,

Y is  or 

in which

R^{14} is hydrogen, halogen, hydroxy or lower alkoxy,

R^{15} is aryloxy, naphthyl, phenyl substituted with substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, halogen, halo(lower)alkyl, hydroxy,

amino(lower)alkyl,
azido(lower)alkyl,
lower alkylamino(lower)alkyl,
acylamino(lower)alkyl,
hydroxy(lower)alkyl, cyano and acyl,
or a heterocyclic group, and

R^{16} is aryl,

and

n is 0, 1, 2 or 3,

or its pharmaceutically acceptable salt for treating and/or preventing Meniere's syndrome or motion sickness.

2. A use of the compound defined in Claim 1 as an agent for treating and/or preventing Meniere's syndrome or motion sickness.

3. An agent for treating and/or preventing Meniere's syndrome or motion sickness, which comprises the compound defined in Claim 1.

4. A method for treating and/or preventing Meniere's syndrome or motion sickness, which comprises administering the compound defined in Claim 1 to mammals.

5. A use of the compound defined in Claim 1 for manufacturing a medicament for treating and/or preventing Meniere's syndrome or motion sickness.

6. A pharmaceutical composition for treating and/or preventing Meniere's syndrome or motion sickness, which comprises the compound defined in Claim 1 in admixture with a carrier or excipient.

7. A Process for preparing the pharmaceutical composition

of Claim 6, which is characterized by admixing the compound with a carrier or excipient.